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## [Commentary] Recognising the Rheumatological Needs of Neurodivergent Females

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### Abstract

We experience life and interact with others in a multitude of ways. The term 'neurodivergence' refers to variations from what is considered typical or normal. Neurodivergence influences an individual's behaviour in social situations and is associated with atypical emotional responses. This can precipitate inequity and rejection. Neurodivergent females experience many physical and psychological health issues, and musculoskeletal disorders account for a significant proportion of these. Research and education into neurodivergent conditions in females should inform the reassessment of clinicians' present approach to those who present with multiple unexplained symptoms. Obtaining official confirmation of a neurodivergent condition improves access to support services and helps them and their family better understand themselves and the challenges they face. This commentary highlights the increased risk of developing rheumatological disease for females with neurodivergent conditions and suggests how clinicians might increase their awareness of this.

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## Key Lessons

1. Neurodivergent conditions are under-recognised among females who often present differently to males.
2. Neurodivergent females are at increased risk of developing a wide range of rheumatological disorders.
3. These include fibromyalgia, hypermobility, rheumatoid arthritis, osteoporosis and connective tissue disease.

## *What is neurodivergence?*

While 'neurodiversity' represents the wide variation in the approach people take when communicating and socialising<sup>[1]</sup>, the term 'neurodivergence' relates more specifically to differences in mental or neurological functioning from the standard norm. This includes autism, ADHD and Tourette's syndrome, and there is evidence that a milder form of neurodivergence accounts for dyslexia and dyspraxia<sup>[2]</sup>. Social isolation and self-harm are common among females with these conditions, and their physical symptoms may in part reflect emotional distress. If we are to better respond to the clinical needs of females with neurodivergent conditions, we need to improve our understanding of their way of thinking and behaving. The ability to describe their feelings may differ significantly from that of neurotypicals. They might struggle to verbalise their symptoms in a logical or consistent manner, and neurodivergent people may find it hard to deal with questions that try to disentangle what may sometimes seem like a jumble of symptoms without a firm timeline. Their expectations of a clinical consultation can differ to that of the clinician, but it is important that doctors recognise this. We should concentrate on the issues that neurodivergent people describe, rather than the problems that they are<sup>[3]</sup>. Obtaining official confirmation of a neurodivergent condition improves access to support services and helps them and their family better understand

themselves and the challenges they face. This commentary highlights the increased prevalence of rheumatological disease in females with neurodivergent conditions, describes these associations and suggests how rheumatologists can help.

### *The link between female neurodivergence and heightened healthcare needs*

Although neurodivergent conditions have been perceived as being the province of males, recent evidence has emerged over the last ten years that challenges this assumption [4]. It appears that although females often receive their diagnosis later in life, ADHD and autism may be much more prevalent among females than has been appreciated. This may be due to their ability to camouflage their difficulties to avoid social rejection or alienation. Because of this, neurodivergent females are more likely to internalise their concerns, resulting in a suppression of their natural tendencies. Such behaviour can trigger intense anxiety, obsession and anger which may manifest itself in a variety of clinical expressions. They can exhibit heightened sensitivity to emotional and sensory stimuli and find that this causes increased muscle tension and tenderness, producing distress and discomfort [5]. Physical symptoms are probably partly genetic and partly environmental in origin. These cause pain and diminished function and need to be recognized and taken seriously. If these features are combined with difficulty in making and maintaining close contact with others, a sense of isolation or abandonment may ensue. Frequently this can cause neurodivergent females to feel misunderstood and to lose faith in their own ability, and to lose confidence in other people's willingness to support them. Autonomic hypersensitivity can be associated with emotional instability and produce a perceived lack of object constancy [6]. Fatigue, muscle tenderness and despair may develop, precipitating a referral to mental health services, the pain team or a rheumatologist.

Autistic people die younger and are more likely to develop a wide range of disorders than their neurotypical peers during their lifetimes [7][8]. A recent review of the literature defined these disorders in detail [9]. Neurodivergent females appear to have worse health care outcomes if they have experienced significant adverse experiences during childhood. Females are at greater risk in this regard, and this might explain their increased use of health care resources [10]. A recent review explored the issues described by autistic females with regards to accessing medical care and identified impaired executive function, poor communication, and hypersensitivity as all being contributory [11]. Failure of health care workers to appreciate these problems led to lower levels of satisfaction and worsening health care outcomes [12]. Surprisingly little literature exists specifically on the needs of females with neurodivergent conditions, despite dysfunction of every organ system being listed among the many disorders they report. However, it is established that autistic females are over-represented among all women who seek support for many medical disorders, and it appears that this is especially true for musculoskeletal conditions.

### *The musculoskeletal healthcare needs of neurodivergent females*

Hypermobility spectrum disorders include Ehlers-Danlos (EDS) which is strongly related to the presence of neurodivergence, especially in females [13]. A reduced sense of balance and poor coordination are often also observed

and may add to the risk of injury, dislocation, or fracture. Formal assessment of the extent of hypermobility using Beighton's test is recommended to quantify joint laxity, which tends to reduce over time. Teaching proprioceptive exercises and the practice of non-weightbearing exercises such as swimming or cycling can be very helpful, especially when allied to the provision of supportive physiotherapy and joint care techniques. A minority of patients are at risk of vascular complications associated with more severe forms of EDS.

Chronic musculoskeletal pain with tenderness to touch and profound fatigue can lead to the suspicion of fibromyalgia in females. This is supported by the presence of autonomic hypersensitivity, which may manifest as postural orthostatic tachycardia syndrome, irritable bowel or recurrent headache. Patients frequently report trouble sleeping and complain of brain fog. Many such women have features of a neurodivergent condition [14] and there maybe also be a family history of autism, ADHD or fibromyalgia" [15][16]. Hypermobility EDS is also often associated with this symptom complex, and it has been postulated that hypermobility mediates the relationship between fibromyalgia and neurodivergence [13][14][16]. Adolescent females with neurodivergent features exhibit more pain than their peers [17], and one report suggested that 77% of young women with autism or ADHD had already manifested features of chronic pain by the age of 27 [18].

Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are among the auto-immune disorders reported with greater frequency in the first degree relatives of neurodivergent females [19]. There is also an increased prevalence of auto-immune conditions among the mothers of neurodivergent women [19][20][21][22]. In addition to maternal auto-immune thyroid disease, both RA [20] and SLE [21][22] are recorded with greater frequency in mothers of neurodivergent female offspring. While maternal RA is associated with a generalised increase in the risk of autism among progeny, maternal SLE is linked to an increased risk for autism only among Caucasian women [23]. The chances of developing both autism and ADHD are increased among the offspring of mothers with RA [24]. Postulated mechanisms for this include neonatal hypoglycaemia and maternal hyperglycaemia [25]. Chronic inflammatory conditions, such as lupus and rheumatoid arthritis, or the use of corticosteroids, may increase maternal glucose levels, exposing the embryo and the fetus to high-glucose concentrations. Intrauterine hyperglycemia, hyperinsulinemia or both may affect neurogenesis. Raynaud's phenomenon may predict or herald the development of a systemic rheumatological auto-immune disorder in neurodivergent female offspring of a mother with auto-immune disease and can be exacerbated by stimulants prescribed for concomitant ADHD [26].

Children with autism exhibit lower bone mineral density across all sites when compared to neurotypical controls [27]. Osteoporosis is reported in females with ADHD, and this may be in part a consequence of prescribed stimulants [28]. Bone loss, or reduced bone formation, along with poor balance due to impaired proprioception, causes a much-inflated fracture risk at the hip, spine, and forearm in autistic females at all ages. Their odds ratio for hip fractures increases from 8.1 in girls to 24.8 in adult autistic females [29]. Other factors that may contribute to this increased fracture risk include vitamin D deficiency and intestinal dysbiosis from restrictive eating disorders in adolescence.

**Table 1.** Lists the common conditions affecting musculoskeletal health experienced by neurodivergent females.

To show the common musculoskeletal conditions experienced by neurodivergent females:
Hypermobility syndromes
Fibromyalgia
Rheumatoid arthritis
Connective tissue disease
Osteoporosis

## *Therapeutic challenges*

Doctors have been slow to recognise the physical features that neurodivergent conditions can manifest in females. Not all females with autism or ADHD are aware of their condition, and those that are neurodivergent may chose not to disclose this. Historically, a label of psychosomatic illness has often been applied to females who exhibit these features, with the concept that such patients can be hard to help. It is time we re-evaluated this approach and adopted a less judgemental attitude. Consistency and continuity of care are important in building the trust which neurodivergent people often struggle to achieve. If a diagnosis of a neurodivergent condition is suspected, access to appropriate multidisciplinary support may be appreciated whilst avoiding unnecessary multiple cross- referrals.

A careful explanation of the diagnosis and its relationship to other aspects of the individual's symptomatology is especially important for neurodivergent females. They need to feel believed and validated in their symptomatology. Even if their condition proves difficult to treat, it is vital that they feel understood and supported both within the consultation and subsequently. Sharing their story verbatim in the letter to their primary care physician can be helpful, especially if they also receive a copy. This also helps to avoid misunderstanding and to help ensure that agreed therapeutic plans are followed through. Obtaining consent for the involvement of other members of the multi-disciplinary team is important where this is proposed. Sharing selective and relevant information on the patient's condition with specialist nurses, physiotherapists or occupational therapists requires the patient's knowledge and consent and will likely improve the effectiveness of the intervention.

Many neurodivergent females describe difficulty in tolerating analgesia<sup>[30]</sup>. They are more prone to side effects and may experience these at lower doses than neurotypical women<sup>[31]</sup>. Starting with a low dose and titrating slowly upwards is a good rule. Certain analgesics also appear to be less effective in autistic females<sup>[32]</sup>, while other agents used off-licence are reported as being useful in relieving pain and distress<sup>[33]</sup>. We may need to reconsider our definition of pain in the setting of neurodivergence, given that functional magnetic resonance imaging demonstrates different cerebral responses in neurodivergent females to their neurotypical peers. Likewise, immunomodulators may be effective at lower than usual doses in neurodivergent females and consensus between the rheumatologist and patient is essential to ensure effective compliance with drug therapy. Access to a helpline is much appreciated by neurodivergent females, especially if there is the option to use email rather than insist on a telephone call<sup>[34]</sup>. Depression may be associated with a sense of isolation, as well as with fatigue and despair. Neurodivergence is a risk factor for both anxiety and depression and antidepressants can improve the quality of life of some subjects with neurodivergence<sup>[35]</sup>.

Within a rheumatological setting, it is important for clinicians to acquire an appreciation of the range of common disorders experienced by neurodivergent females. The art of 'learning to listen' remains an essential tool in diagnosis.

Neurodivergent people can feel uncomfortable if they are not given enough time to share their concerns, and an open unhurried dialog is more likely to facilitate a diagnosis. If patients are encouraged to share their lived experience, it becomes easier for the clinician to 'join the dots', which may allow the diagnosis of a neurodivergent condition to surface from what may have previously appeared to be a random collection of unrelated symptoms. Likewise, it is essential that clinicians are aware of the broad range of rheumatic conditions commonly experienced by neurodivergent females. If we are to become more effective at managing these conditions, breaking down barriers between services for physical and mental health would be a great help. This may allow the relationship between the limbic, endocrine, and immune systems in neurodivergent individuals to be more fully understood.

### *How patients and the public contributed to this article*

Two of the authors of this paper have lived experience of female neurodivergence, and two authors work in the provision of health care delivery to females with neurodivergent conditions. Females with autism and / or ADHD specifically requested that we emphasise and explain their medical needs to Rheumatologists to improve their access to effective healthcare.

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*Each of the authors discussed, designed, wrote and reviewed the manuscript.*

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